

an effective dose of a glucagon-like peptide-1 (GLP-1) molecule to the lungs of a patient suffering from hyperglycemia, wherein the GLP-1 molecule has an amino acid sequence of a formula:

R_1 -X-Glu-Gly-Thr-Phe-Thr-Ser-Asp-Val-Ser-Ser-Tyr-Leu-Y-Gly-
Gln-Ala-Ala-Lys-Z-Phe-Ile-Ala-Trp-Leu-Val-Lys-Gly-Arg- R_2
(SEQ ID NO:1)

wherein:

R_1 is selected from the group consisting of L-histidine, D-histidine, desamino-histidine, 2-amino-histidine, beta-hydroxy-histidine, homohistidine, alpha-fluoromethyl-histidine, and alpha-methyl-histidine;

X is selected from the group consisting of Gly, Val, Thr, Ile, and alpha-methyl-Ala;

Y is selected from the group consisting of Glu, Gln, Ala, Thr, Ser, and Gly;

Z is selected from the group consisting of Glu, Gln, Ala, Thr, Ser, and Gly; and

R_2 is selected from the group consisting of NH_2 , and Gly-OH.

134. (amended) The method of **Claim 128**, wherein the GLP-1 molecule is delivered from an inhalation device selected from the group consisting of a nebulizer, a metered-dose inhaler, a dry powder inhaler, and a sprayer.

142. (amended) The method of **Claim 140**, wherein the GLP-1 molecule is delivered from an inhalation device selected from the group consisting of a nebulizer, a metered-dose inhaler, and a sprayer

144. (amended) A method of normalizing blood glucose comprising administering an effective dose of a GLP-1 molecule to the lungs of a patient suffering from

hyperglycemia, wherein the GLP-1 molecule is GLP-1(7-34), GLP-1(7-35), GLP-1(7-36), or GLP-1(7-37), or the amide forms thereof, comprising at least one modification selected from the group consisting of:

- (a) substitution of a glycine, serine, cysteine, threonine, asparagine, glutamine, tyrosine, alanine, valine, isoleucine, leucine, methionine, phenylalanine, arginine, or D-lysine for lysine at position 26 and/or position 34 or substitution of a glycine, serine, cysteine, threonine, asparagine, glutamine, tyrosine, alanine, valine, isoleucine, leucine, methionine, phenylalanine, lysine, or a D-arginine for arginine at position 36;
- (b) substitution of an oxidation-resistant amino acid for tryptophan at position 31;
- (c) substitution according to at least one of:
Y for V at position 16;
K for S at position 18;
D for E at position 21;
S for G at position 22;
R for Q at position 23;
R for A at position 24; and
Q for K at position 26;
- (d) substitution comprising at least one of:
glycine, serine, or cysteine for alanine at position 8;
aspartic acid, glycine, serine, cysteine, threonine, asparagine, glutamine, tyrosine, alanine, valine, isoleucine, leucine, methionine, or phenylalanine for glutamic acid at position 9;
serine, cysteine, threonine, asparagine, glutamine, tyrosine, alanine, valine, isoleucine, leucine, methionine, or phenylalanine for glycine at position 10; and
glutamic acid for aspartic acid at position 15; and
substitution glycine, serine, cysteine, threonine, asparagine, glutamine, tyrosine, alanine, valine, isoleucine, leucine, methionine, or phenylalanine or the D or N-acylated or alkylated form of histidine for

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Cont.

B4 conclude

histidine at position 7.

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155. (amended) The method of **Claim 149**, wherein the GLP-1 molecule is delivered from an inhalation device selected from the group consisting of a nebulizer, a metered-dose inhaler, a dry powder inhaler, and a sprayer.

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163. (amended) The method of **Claim 160**, wherein the GLP-1 molecule is delivered from an inhalation device selected from the group consisting of a nebulizer, a metered-dose inhaler, and a sprayer.

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165. (amended) A method of normalizing blood glucose comprising administering an effective dose of a GLP-1 molecule to the lungs of a patient suffering from hyperglycemia, wherein the GLP-1 molecule is a GLP-1 derivative prepared by the process of acylating a GLP-1 analog selected from the group consisting of GLP-1(7-34), GLP-1(7-35), GLP-1(7-36), and GLP-1(7-37), or the amide forms thereof, comprising at least one modification selected from the group consisting of:

- (a) substitution of a glycine, serine, cysteine, threonine, asparagine, glutamine, tyrosine, alanine, valine, isoleucine, leucine, methionine, phenylalanine, arginine, or D-lysine for lysine at position 26 and/or position 34 or substitution of a glycine, serine, cysteine, threonine, asparagine, glutamine, tyrosine, alanine, valine, isoleucine, leucine, methionine, phenylalanine, lysine, or a D-arginine for arginine at position 36;
- (b) substitution of an oxidation-resistant amino acid for tryptophan at position 31;
- (c) substitution according to at least one of:
 - Y for V at position 16;
 - K for S at position 18;
 - D for E at position 21;
 - S for G at position 22;
 - R for Q at position 23;

R for A at position 24; and

Q for K at position 26;

- (d) substitution comprising at least one of:
- glycine, serine, or cysteine for alanine at position 8;
 - aspartic acid, glycine, serine, cysteine, threonine, asparagine, glutamine, tyrosine, alanine, valine, isoleucine, leucine, methionine, or phenylalanine for glutamic acid at position 9;
 - serine, cysteine, threonine, asparagine, glutamine, tyrosine, alanine, valine, isoleucine, leucine, methionine, or phenylalanine for glycine at position 10; and
 - glutamic acid for aspartic acid at position 15; and
 - substitution glycine, serine, cysteine, threonine, asparagine, glutamine, tyrosine, alanine, valine, isoleucine, leucine, methionine, or phenylalanine or the D or N-acylated or alkylated form of histidine for histidine at position 7.

E9
Conclude

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168. (amended) The method of ~~Claim 167~~ wherein the GLP-1 molecule is in the form of a dry powder.

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174. (amended) The method of ~~Claim 168~~ wherein the GLP-1 molecule is delivered from an inhalation device selected from the group consisting of a nebulizer, a metered-dose inhaler, a dry powder inhaler, and a sprayer.

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180. (amended) The method of ~~Claim 167~~, wherein the GLP-1 molecule is administered as an aerosol.

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182. (amended) The method of ~~Claim 173~~, wherein the GLP-1 molecule is delivered from an inhalation device selected from the group consisting of a nebulizer, a metered-dose inhaler, and a sprayer.

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184. A method of normalizing blood glucose comprising administering an effective dose of a GLP-1 molecule to the lungs of a patient suffering from hyperglycemia, wherein the GLP-1 molecule is a GLP-1 analog with alanine at position 8 substituted with an amino acid selected from the group consisting of valine, glycine, or alpha-methyl alanine.

185. The method of **Claim 184** wherein alanine at position 8 is substituted with valine.

186. The method of **Claim 184** wherein alanine at position 8 is substituted with glycine.

187. The method of **Claim 185** wherein the GLP-1 molecule is in the form of a dry powder.

188. The method of **Claim 187** wherein the GLP-1 molecule is delivered from an inhalation device selected from the group consisting of a nebulizer, a metered-dose inhaler, a dry powder inhaler, and a sprayer.

189. The method of **Claim 185**, wherein the GLP-1 molecule is administered as an aerosol.

190. The method of **Claim 189**, wherein the GLP-1 molecule is delivered from an inhalation device is selected from the group consisting of a nebulizer, a metered-dose inhaler, and a sprayer.

191. The method of **Claim 186** wherein the GLP-1 molecule is in the form of a dry powder.